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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/712,525	11/14/2000	Salvatore J. Salamone	RDID00111US	9732

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EXAMINER
LUCAS, ZACHARIAH

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/712,525	SALAMONE, SALVATORE J.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *7-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in the paper filed on November 13, 2003 is acknowledged. The traversal is on the ground(s) that the kits described in the claims may not be used for the identification of agonists or antagonists in a sample. This is not found persuasive because, while the Applicant's argument may be persuasive with reference to a sample to be studied, the reason for finding the kit and the methods need not be restricted to the kits use with reference to a particular sample type. In this case, the kit may both be used to identify HIV protease inhibitors in a sample from a patient, and in methods for the general identification of agonists or antagonists to such inhibitors by mixing the kits components with the inhibitor and the putative agonist/antagonist and determining the effects of the putative agent on the inhibitors ability to bind the kit components. Thus, the kit has uses other than in the claimed methods.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 7-11 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the paper filed on November 19, 2003.

3. Currently, claims 1-6 are pending and under consideration in the application.

Information Disclosure Statement

4. The information disclosure statements (IDS) submitted on May 4, 2001, and July 22, 2002, are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner.

Specification

5. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: It is required that the Applicant amend the specification to provide antecedent basis for the subject mater of claim 6. It is suggested that the language of the claim be introduced into the portion of the specification referring to this method (page 4, lines 6-9).

6. The disclosure is objected to because of the following informalities: the Dorn application referred to on page 4 of the application has now issued as patent number 6,524,808. It is requested that the Applicant amend the application to reflect the change in status of the referenced application.

Appropriate correction is required.

Claim Objections

7. Claim 6 is objected to because of the following informalities: the claim refers to the compounds IMP, NAD, IMPDH, and NADH without first identifying the compounds by their complete names. Appropriate correction is required.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is treated as representative. This claim described an immunoassay for the detection of an HIV protease inhibitor in a sample by combining a sample with a receptor specific for the inhibitor (receptor), a conjugate of a ligand to the inhibitor and a label (conjugate), and measuring the amount of receptor bound to the conjugate. It is unclear what the applicant is claiming. It is noted that the specification describes alternative methods of detecting HIV protease inhibitors; a competition assay, and a sandwich assay. Page 3, lines 4-10. In the present claims, the applicant appears to be claiming a sandwich assay wherein, if the test sample comprises the target inhibitor, the receptor will bind the inhibitor, which will in turn bind to the ligand- thereby allowing for the detection of the label conjugated thereto.

However, the claims indicate that what is being detected in the methods is the label of the conjugates bound to the receptor, rather than a complex of the receptor, inhibitor and conjugate. Thus, the claims are indicating the ligand binds not to the HIV protease inhibitor, but to the receptor itself. In such a case, it would appear that the ligand of the claim is not a ligand to the inhibitor, but a ligand to the receptor- another inhibitor or a analog thereof. The claims are therefore unclear because, while the components of the claimed method appear to be those of a

sandwich assay, the method of detection appears to be that of a competitive assay. Clarification of what is being claimed is required.

For the purposes of this action, because the claims indicate that the ligand is a ligand of the protease inhibitor, the claims are being treated as reading on sandwich assays for the protease inhibitors.

10. Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This claim further limits the methods of claim 1 to embodiments wherein the "signal generating moiety is selected from the group consisting of enzymes, fluorogenic compounds, chemiluminescent materials, electrochemical mediators, particles, reporter groups, enzyme inhibitors, and polypeptide carriers." It is unclear what signal generating moieties are encompassed by the terms "particles" and "polypeptide carriers." Clarification is required.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boguslaski et al. (U.S. Patent 4,134,792, of record in the IDS of July 22, 2002), in view of Remmel et al. (Clin

Chem 46(1): 73-81, May 2001 IDS), Wiltshire et al. (Anal Biochem 281: 105-114, May 2001 IDS), and Vaillancourt et al. (AIDS Res Hum Retroviruses 15: 355-63). The claims read on immunoassays to determine the presence of an HIV inhibitor in a sample. The immunoassays are described as comprising the steps of combining a sample with a receptor specific for said inhibitor and a conjugate comprising a ligand of the inhibitor and a non-radioactive reporter; measuring the amount of said receptor bound to said conjugate by monitoring the production of signal generated by said moiety, and correlating said production of signal with the presence of the inhibitor.

Boguslaski teaches methods of identifying analytes in sample through methods referred to as "homogeneous schemes" for conducting immunoassays in columns 7-8 of the patent. The method does not require the removal of bound and unbound labels. Col. 7, lines 30-45. Further, the reference also teaches that non-radioactive labeling moieties have been developed for use in the homogeneous assays. Col. 1, lines 51-59. Thus, the reference teaches a method comprising the steps of the claimed methods, but does not teach or suggest the use of such methods to detect the presence of HIV protease inhibitors in a sample.

Remmel teaches that methods for determining the presence and amount of HIV-1 protease inhibitors are useful in several instances. Page 80. However, the reference does not teach the use of an immunoassay for such detection. Wiltshire teaches the making and use of antibodies against the HIV-1 protease inhibitor saquinavir. Pages 112-114. Vaillancourt teaches that these inhibitors act through binding to the active region of the proteases, thereby indicating that these proteases are binding partners (ligands or receptors) to the inhibitors. Page 355. However, the references do not teach the use of either the sandwich assay, or the use of non-

radioactive labels. When these references are read in combination with the teachings of Boguslaski, which provides both a motivation to use labels other than radioactive labels, and which teaches the use of the homogeneous sandwich assay, it would have been obvious to those in the art to use such an assay using the antibodies of Wiltshire to detect Saquinavir. These references therefore render the claimed methods obvious.

13. Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Frengen et al. (U.S. Patent 5,739,042) in view of the teachings of Remmel et al. (supra), Wiltshire et al. (supra), and Vaillancourt et al. (supra) and in light of the teachings of Meyerhoff et al. (U.S. Patent 5,830,680). The claims have been described above, as have the teachings of Remmel and Wiltshire.

Frengen teaches the use of sandwich assays for the detection of analytes. Columns 1-2. The reference indicates that two analyte-binding compounds are used, a receptor (which may attached to a solid support such as a microtitre plate) and a labeled ligand. The reference further teaches that a disadvantage of the assay is the need for the separation of bound and unbound analyte. However, as indicated by the teachings of Meyerhoff, this disadvantage is overcome by the use of homogeneous methods of enzyme immunoassays. Columns 1-2. These references do not teach the use of such assays for the detection of HIV-1 protease inhibitors.

The teachings of Wiltshire and Remmel are disclosed above. These references teach the need for, and the use of antibodies in the detection of HIV-1 protease inhibitors. Further, as indicated by Vaillancourt (page 355), it would have been apparent to those in the art that the inhibitors would be capable of binding to the HIV-1 proteases, and thus known that such proteins

could be used as a binding partner for the inhibitor. Thus, the art teaches both receptors and ligands for the inhibitors, the need for means of detecting and quantifying such inhibitors, and methods of detecting and quantifying analytes. It would therefore have been obvious to those in the art to use the methods of Frengen, using an enzyme label, for the detection of HIV-1 protease inhibitors.

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 1-6 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 8-10, 15-18 of Dorn et al. (U.S. Patent No. 6,524,808- Dorn) in view of Remmel. The claims have been described above. Dorn claims a method of determining the amount of a drug in a sample using the method of claim 6. The patent also claims kits for use in the assay. However, the reference does not teach or suggest the use of the assay for the detection of HIV protease inhibitors.

Remmel teaches the need for detection of amounts of such inhibitors in patients, and a separate method for the detection of such inhibitors. Because Dorn teaches that the method

described therein is useful for the detection of drugs generally, and because Remmel teaches the need for methods that can determine the amounts of HIV protease inhibitors in a sample, it would have been obvious to those in the art to have used the method of Dorn to detect and quantify the presence of such inhibitors. As the claims of the Dorn patent are generic to those of the present application, the claim are rejected under the doctrine of obviousness type double patenting as obvious over the Dorn patent in view of Remmel.

Conclusion

16. No claims are allowed.

17. The following prior art references are made of record and are considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

> U.S. Patents 5,160,597, and 6,444,433. These references are relevant in that they teach that those in the art are in possession of the knowledge necessary for the production of antibodies that bind small molecules, such as the HIV-1 protease inhibitors indicated in the claims. 5,160,597, columns 4-5; 6,444,433, column 4.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

2/23/04

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